

Supplementary Table 1. Principles of Radiation in Common Tumours Adjacent to Orbit & Anterior Visual Pathways

Site/Primary tumor	General treatment paradigm (some variations)	RT schedule/dose range (some variations)	Approximate 5y OS or Median OS	Comments
Primary Intracranial Tumors				
Cavernous Sinus and optic nerve sheath meningioma	Surgical debulking if large mass effect, otherwise primarily fx'd RT	Fx'd 45-54 Gy in 1.8-2 Gy Fx daily / 5-6 weeks. Small tumors may be treated with SRS from 12-15 Gy.	92-95% 5y OS	Risk of RION, radionecrosis w SRS doses >18Gy, hypopituitarism, reactive oedema tx w/ steroids, risk of stroke / neurocognitive impairment due to temporal lobe RT.
Atypical or Anaplastic meningioma	Surgery-> fx'd RT with larger margin than grade 1 meningioma	Fx'd 60-66 Gy in 30-33 fx; 1.8-2 Gy/fx / 6-6.5 weeks. RT margins include a CTV margin of 1-2 cm and a PTV margin of 3-10 mm.	20-50 % 5y OS	Surgery important for OS. Postoperative fx'd RT 6 weeks. SRS investigational. For Anaplastic Meningioma, palliative RT if prognosis is poor.
Grade 1 glioma	Observation, resection if safe; Fx'd RT at time of symptomatic progression if unresectable	Fx'd 45-54 Gy in 1.8-2 Gy / Fx daily / 5-6 weeks	>92%	Slow growing tumor; observation often preferred until symptom onset. Due to risk of RT induced malignancy, delayed onset of RT is preferred owing to long life expectancy
Grades 2-4 Glioma	Surgery-> fx'd RT +/- oral temozolomide	Fx'd 45-60 Gy in 1.8-2 Gy / Fx daily / 5-6 weeks. RT margins range from 5mm-2cm of tissue surrounding tumor.	6 months – 9y	IDH mutation, MGMT promoter methylation, age, extent of resection, presence of symptoms, and performance status affect prognosis.
Symptomatic primary CNS tumor or HN Ca	Palliative RT with doses of > 2.2 Gy / Fx.	8 Gy x 1	Median OS estimated <6 months	Palliative RT for symptoms; high dose per Fx in few Fx (hypo-Fx'd).
		4 Gy x 5		
		5 Gy x 5		

with poor prognosis	Hypo-Fx'd (large dose per Fx) from 1-15 treatments	6 Gy x 5 3 Gy x 10 2.5 Gy x 15 "Quadshot" or "0-7-21" regimen		RT given alone due to risk of chemo-RT toxicity. IMRT planning takes significant time; so simple 3D Conformal often used to allow prompt completion.
Clival Chordoma & Chondrosarcoma	Max safe resection then RT, often w/ protons for dose escalation	High dose RT >65 Gy improves outcome. Rx proton therapy, or combo of image guided IMRT, IMPT +/- SRS boost	Clival chordoma 5y OS: 60% chordoma; 80% Chondrosarcoma	Chondrosarcoma: slow growing tumor, may choose resection, and at recurrence, re-resection and RT. Proton therapy may improve ability to deliver high dose in skull base.
Head and Neck Cancers				
Advanced Skin Cancers (eg Basal or Squamous Cell Carcinoma) of the face, eyelid, forehead, nasal skin, temporal skin	Surgery followed by fx'd RT +/- chemo when advanced. Early stage: RT alone	Fx'd 60-70Gy in 30-35 Fx, 1.8-2 Gy / Fx / 6-7 weeks daily.	1y OS 85.7 % 2y OS immuno-suppressed: 36% vs immuno-competent 67%	Survival depends on patient factors, tumor (size, PNI/LVI, PDL1, stage, location) tx factors (extent of resection, indications for RT, chemotherapy). Some tx w/ immunotherapy or monoclonal antibodies (cemiplimab, cetuximab).
Advanced Cancers of the Nasal Cavity and Paranasal Sinuses (frontal, maxillary, ethmoid, sphenoid)	Surgical resection followed by fx'd RT +/- chemotherapy when advanced. Definitive, concurrent chemo-RT when unresectable	Fx'd 60-70Gy in 30-35 Fx, 1.8-2 Gy / Fx / 6-7 weeks daily +/- chemotherapy for risk factors	5y OS: 52% (locoregional SqCCa) Median OS for SMARCB1 deficient Sinonasal CA: 22 months.	Survival depends largely on histology and stage. Most common histologies - SqCCa, Adeno-CA, Small Cell CA, sarcoma, multiphenotypic sinonasal CA, Adenoid Cystic CA, sinonasal undifferentiated CA, SMARCB1 deficient CA, inverted melanoma, olfactory neuroblastoma.
Intermediate Grade Lymphomas (DLBCL, NK-T Cell Lymphomas)	Chemotherapy followed by RT	Fx'd RT 30-55 Gy in 1.8-2 Gy / Fx to involved field	DLBCL 70% 2y, 50% 5y; NK T Cell 3y OS: 30-50%	Survival depends on early response to tx. Common chemo-rituximab, cytoxan, doxorubicin, vincristine, prednisone. For NK-T cell lymphomas, higher dose RT and modified "SMILE" asparaginase, methotrexate, and dexamethasone, cisplatin, ifosfamide, etoposide

Orbital marginal zone lymphoma	RT alone	Fx'd RT to 24-30 Gy in 1.5-2 Gy / Fx	5y OS 100% in many series, LC 92%	Trend toward ultra-low dose (2 Gy x 2 fractions) to avoid toxicity
		2 Gy x 2 Fx to 4 Gy for low grade		
Locally advanced nasopharyngeal SqCCA	chemo->chemo-RT, or chemo-RT->chemotherapy	Fx'd RT to 69-70 Gy in 1.8-2.25 Gy / Fx	5y OS 50-71%	Prognosis depends on disease extent, stage, histology, response to tx. Common chemo: cisplatin / 5-FU
Re-RT cases in the head and neck	surgery followed by RT +/- chemo	Proton or IMRT; standard (1.8-2 Gy / Fx) or hyper-Fx'd (<1.8 Gy / Fx delivered twice daily >6 hours apart)	1y OS: 50% if recurrent; 5y OS 50% if second primary tumor	Prognosis depends on histology, time from last course, survivability of complications (fibrosis, radiation necrosis, carotid blowout, fistula, wound healing, infection)

Fx: Fraction. Fx'd: Fractionated. Standard Fractionation: when dose per fraction is 1.8-2 Gy. Hypofractionated: when dose per fraction is > 2 Gy and completed over a short course. Hyperfractionated: dose per fraction is < 1.8 Gy and often given more than once per day (eg twice daily > 6 hours apart), often used in the setting of re-irradiation in head and neck cancer. RT: Radiotherapy. Chemo-RT: Concurrently delivered chemotherapy and radiation Gy: Gray. SRS or SBRT: stereotactic radiosurgery (inside the CNS) or stereotactic body radiotherapy (outside the CNS) where high doses per fraction are given to a small volume for ablative dose, between 1-5 fractions. CA: carcinoma. BED: Biologically Effective Dose. BED Equation: $BED = nd [1 + (d / \alpha\beta)]$ - where n= number of fractions, d=dose per fraction, and $\alpha\beta$ = the alpha/beta ratio for the tissue of interest. Optic structure toxicity has an $\alpha\beta$ of approximately 2, whereas skin toxicity is approximately 10. Useful for calculating safe dose constraints particularly for re-irradiation respecting normal tissue tolerances. OS: Overall Survival. PNI: Perineural Invasion. LVI: Lymphovascular Invasion. Hx: History. Tx: Therapy. Y: year. SqCCA: Squamous Cell Carcinoma